K130255

FEB 2 8 2014

510(k) Summary (Summary of Safety and Effectiveness)

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

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Date Summary prepared: January 31, 2013 Revised February 25, 2014

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2. Device Name

Hemoglobin A_{1c}
Hemoglobin A_{1c} Calibrators
Hemoglobin A_{1c} Controls

Reagents

Classification Name: Assay, Glycosylated Hemoglobin
Regulation Description: Glycosylated hemoglobin assay
Trade Name: Hemoglobin A_{1c}
Common Name: HbA_{1c}
Governing Regulation: 862.1373
Device Classification: Class II
Product Code: PDJ, LCP
Panel Classification: Chemistry

Calibrators

Classification Name: Calibrator, Secondary
Regulation Description: Calibrator
Trade Name: Hemoglobin A_{1c} Calibrators (1 and 2)
Common Name: Calibrator
Governing Regulation: 862.1150
Device Classification: Class II
Product Code: JIT
Panel Classification: Clinical Chemistry

Controls

Classification Name: Single (Specified) Analyte Controls (assayed and unassayed)
Regulation Description: Quality control material (assayed and unassayed)
Trade Name: Hemoglobin A_{1c} Controls (Low and High)
Common Name: Control
Governing Regulation: 862.1660
Device Classification: Class II
Product Code: JJX
Panel Classification: Clinical Chemistry

3. Predicate Device

Reagents

COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay (k121291)

Calibrators

Roche C.f.a.s. (Calibrator for Automated Systems) HbA1c (k052101)

Controls

Roche PreciControl HbA1c norm and PreciControl HbA1c path (k103099)

4. Description of Device

Reagents

The Hemoglobin A_{1c} Reagent Kit contains:

Component	Number of Bottles x Volume
Reagent 1 (R1)	1 x 52 mL
Reagent 2 (R2)	1 x 20 mL
Diluent (A1cDIL)	2 x 35 mL

Estimated tests per kit: 300
Calculation is based on the minimum fill volume per kit.

Reagent	Reactive Ingredients	Concentration
Reagent 1	10-(carboxymethylaminocarbonyl)-3,7-bis(dimethylamino) phenothiazine sodium salt	0.000817%
	Protease (Bacterial)	< 1 mU/dL
Reagent 2	Peroxidase (Horseradish)	5 to 15 kU/dL
	Fructosyl-peptide-oxidase (*E. coli*, recombinant)	300 to 900 U/dL
Diluent	Sodium nitrite	> 0.05 to < 0.3%

Inactive Ingredients: Reagent 1 contains sodium azide as a stabilizer and preservative. Reagent 1 and Diluent contain ProClin 300 as a preservative. Reagent 2 contains ofloxacin as a preservative.

Calibrators

The Hemoglobin A_{1c} Calibrator Kit contains:

Component	Number of Bottles x Volume
Calibrator 1 (Cal 1)	1 x 1.6 mL*
Calibrator 2 (Cal 2)	1 x 1.6 mL*

* Volume after reconstitution

- A1c Calibrators (lyophilized) contain hemoglobin and glycated hemoglobin from human whole blood. Prior to lyophilization, the calibrator matrix is an MES-buffered solution. Preservative: Ofloxacin.
- The value-assigned A1c Calibrator values are within the following hemoglobin A_{1c} ranges:

	Calibrator 1	Calibrator 2
Hemoglobin A_{1c} Ranges	4.59% to 6.02% HbA_{1c}	10.52% to 13.37% HbA_{1c}

- Actual analyte concentrations for each lot of calibrators are listed in the Hemoglobin A_{1c} Calibrator Value Sheet, packaged with the calibrator.
- Each lot of calibrators is value-assigned. The concentration of glycated hemoglobin (HbA_{1c}) and total hemoglobin (THb) is provided for each lot. Calibrators are prepared gravimetrically, lyophilized, and then value assigned using secondary calibrators that are traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) reference method.

Controls

The Hemoglobin A_{1c} Control Kit contains:

Component	Number of Bottles x Volume
Low Control (Control L)	1 x 1 mL*
High Control (Control H)	1 x 1 mL*

* Volume after reconstitution

- A1c Controls (lyophilized) contain hemoglobin and glycated hemoglobin from human whole blood. Prior to lyophilization, the control matrix is an MES-buffered solution. Preservative: Ofloxacin.
- The value-assigned A1c Control values are within the following hemoglobin A_{1c} ranges:

	Low Control	High Control
Hemoglobin A_{1c} Ranges	4.59% to 6.02% HbA_{1c}	9.42% to 11.07% HbA_{1c}

- Actual analyte concentration ranges for each lot of controls is listed in the Hemoglobin A_{1c} Control Value Sheet, packaged with the controls.
- Each lot of controls is value-assigned. The glycated hemoglobin value in National Glycohemoglobin Standardization Program (NGSP) units (%HbA_{1c}) and in International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) units (mmol/mol HbA_{1c}) are provided for each lot. Controls are prepared gravimetrically, lyophilized, and then value assigned using secondary calibrators that are traceable to the IFCC reference method.

Principles of the Procedure

The Hemoglobin A_{1c} assay consists of two separate concentration measurements: glycated hemoglobin (HbA_{1c}) and total hemoglobin (THb). The two concentrations are used to determine the percent HbA_{1c} (NGSP units) or the hemoglobin fraction in mmol/mol (IFCC units).

The individual concentration values of HbA_{1c} and THb generated by the Hemoglobin A_{1c} assay are used only for calculating the percent hemoglobin A_{1c} or HbA_{1c} fraction, and must not be used individually for diagnostic purposes.

The anticoagulated whole blood specimen is lysed automatically on the system for the Whole Blood application or may be lysed manually using the Hemoglobin A_{1c} Diluent (A1cDIL) for the Hemolysate application.

Glycated Hemoglobin (HbA_{1c})

The Hemoglobin A_{1c} assay utilizes an enzymatic method that specifically measures *N*-terminal fructosyl dipeptides of the β-chain of HbA_{1c}.

- In the pretreatment process, the erythrocytes are lysed and the hemoglobin is transformed to methemoglobin by reaction with sodium nitrite.
- With the addition of Reagent 1 (R1) to the sample, the glycosylated *N*-terminal dipeptide (fructosyl-VH) of the β-chain of hemoglobin is cleaved by the action of protease. The hemoglobin is transformed to stable methemoglobin azide by the action of sodium azide and the concentration of the hemoglobin is determined by measuring absorbance.

- Addition of Reagent 2 (R2) starts a reaction and fructosyl peptide oxidase (FPOX) is allowed to react with fructosyl-VH. The HbA_{1c} concentration is measured by determining the resultant hydrogen peroxide.

Total Hemoglobin (THb)

The hemoglobin is oxidized to stable methemoglobin azide by the action of sodium nitrite and sodium azide and the concentration of the hemoglobin is determined by measuring absorbance (sample + R1).

Hemoglobin A_{1c} Calculations

The final result is expressed as $\%HbA_{1c}$ (NGSP) or mmol/mol HbA_{1c} (IFCC) and is automatically calculated by the system from the HbA_{1c}/THb ratio as follows:

mmol/mol HbA_{1c} IFCC:
HbA_{1c} (mmol/mol) = (HbA_{1c}/THb) × 1000

$\%HbA_{1c}$ DCCT/NGSP:
HbA_{1c} (%) = IFCC x 0.09148 + 2.152

Methodology: Enzymatic

5. Intended Use of Device

The Hemoglobin A_{1c} assay is used in clinical laboratories for the quantitative *in vitro* measurement of percent hemoglobin A_{1c} (NGSP) or HbA_{1c} fraction mmol/mol (IFCC) in human whole blood and hemolysate on the ARCHITECT *c* 8000 System.

Hemoglobin A_{1c} measurements are used as an aid in the diagnosis of diabetes mellitus, as an aid to identify patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus.

The Hemoglobin A_{1c} Calibrators are for use in the calibration of the Hemoglobin A_{1c} assay on the ARCHITECT *c* 8000 System.

The Hemoglobin A_{1c} Controls are used for the estimation of test precision and the detection of systematic analytical deviations of the Hemoglobin A_{1c} assay on the ARCHITECT *c* 8000 System.

WARNING: The Hemoglobin A_{1c} assay has significant interference with the fetal hemoglobin (HbF). Hemoglobin A_{1c} results are invalid for patients with abnormal amounts of HbF, including those with known Hereditary Persistence of Fetal Hemoglobin.

6. Comparison of Technological Characteristics

The Hemoglobin A_{1c} assay (candidate assay) utilizes an enzymatic methodology for the quantitative *in vitro* measurement of percent hemoglobin A_{1c} or HbA_{1c} fraction and is intended for use on the ARCHITECT *c* 8000 System. The COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay is an *in vitro* diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A_{1c} (IFCC) and % hemoglobin A_{1c} (DCCT/NGSP) in hemolysate or whole blood on the Roche COBAS INTEGRA 800 clinical chemistry analyzer.

The following table provides the similarities and differences between the candidate assay and the predicate assay.

Reagent Similarities and Differences		
Characteristics	**Submission Device Hemoglobin A_{1c}**	**Predicate Device COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 (k121291)**
Intended Use and Indications for Use	For the quantitative *in vitro* measurement of percent hemoglobin A_{1c} (NGSP) or HbA_{1c} fraction mmol/mol (IFCC) in human whole blood and hemolysate on the ARCHITECT *c* 8000 System. Hemoglobin A_{1c} measurements are used as an aid in the **diagnosis** of diabetes mellitus, as an aid to identify patients who may be at risk for developing diabetes mellitus, and for the **monitoring** of long-term blood glucose control in individuals with diabetes mellitus.	This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. The COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay is an in vitro diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on the Roche COBAS INTEGRA 800 clinical chemistry analyzer.
Platform	ARCHITECT *c* 8000 System (clinical chemistry analyzer)	Roche COBAS INTEGRA 800 (clinical chemistry analyzer)
Methodology	Enzymatic	Immunoassay
Specimen Type	<u>Whole blood and Hemolysate:</u> Dipotassium EDTA Lithium Heparin Sodium Heparin Sodium Fluoride/Disodium EDTA Tripotassium EDTA	<u>Whole blood and Hemolysate:</u> Li-Heparin K2-EDTA K3-EDTA KF/Na_2-EDTA Na-Heparin NaF/K-oxalate NaF/Na_2-EDTA

<table>
<tr><th colspan="3">Reagent
Similarities and Differences</th></tr>
<tr><th>Characteristics</th><th>Submission Device
Hemoglobin A_{1c}</th><th>Predicate Device
COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 (k121291)</th></tr>
<tr><td>Expected Values</td><td>For monitoring diabetic patients, it is recommended that glycemic goals are individualized following current professional society recommendations. The American Diabetes Association (ADA) recommendations are summarized in the following table.
<table><tr><th>HbA_{1c} Value</th><th>Glycemic Goal</th></tr><tr><td>< 8 %HbA_{1c} (64 mmol/mol)</td><td>Less Stringent</td></tr><tr><td>< 7 %HbA_{1c} (53 mmol/mol)</td><td>General (Non-Pregnant Adults)</td></tr><tr><td>< 6.5 %HbA_{1c} (48 mmol/mol)</td><td>More stringent</td></tr></table>HbA_{1c} values above 6.5 %HbA_{1c} (48 mmol/mol) are an indication of hyperglycemia during the preceding 2 to 3 months or longer. According to the recommendations of the ADA, HbA_{1c} values above 6.5 %HbA_{1c} (48 mmol/mol) are suitable for the diagnosis of diabetes mellitus. Patients with HbA_{1c} values in the range of 5.7 - 6.4 %HbA_{1c} (39 - 46 mmol/mol) may be at a risk of developing diabetes.</td><td>Protocol 1 (acc. to IFCC): 20-42 mmol/mol HbA1c
Protocol 2 (acc. to DCCT/NGSP): 4.0-6.0 % HbA1c

HbA1c levels higher than the upper end of this reference range are an indication of hyperglycemia during the preceding 2 to 3 months or longer. According to the recommendations of the American Diabetes Association values above 48 mmol/mol HbA1c (IFCC) or 6.5 % HbA1c (DCCT/NGSP) are suitable for the diagnosis of diabetes mellitus. Patients with HbA1c values in the range of 39-46 mmol/mol HbA1c (IFCC) or 5.7-6.4 % HbA1c (DCCT/NGSP) may be at a risk of developing diabetes.

HbA1c levels may reach 195 mmol/mol (IFCC) or 20 % (DCCT/NGSP) or higher in poorly controlled diabetes. Therapeutic action is suggested at levels above 64 mmol/mol HbA1c (IFCC) or 8 % HbA1c (DCCT/NGSP). Diabetes patients with HbA1c levels below 53 mmol/mol HbA1c (IFCC) or 7 % HbA1c (DCCT/NGSP) meet the goal of the American Diabetes Association.

HbA1c levels below the established reference range may indicate recent episodes of hypoglycemia, the presence of Hb variants, or shortened lifetime of erythrocytes.</td></tr>
<tr><td>Measuring Interval</td><td>4.0 to 14.0 %HbA_{1c} (DCCT/NGSP)
20.22 to 129.51 mmol/mol HbA_{1c} (IFCC)</td><td>4.2 to 20.1% HbA1c (DCCT/NGSP)
23 to 196 mmol/mol HbA1c (IFCC)</td></tr>
</table>

Calibrator Similarities and Differences		
Characteristics	**Submission Device Hemoglobin A_{1c}**	**Predicate Device Roche C.f.a.s. HbA1c (k052101)**
Intended use	For use in the calibration of the Hemoglobin A_{1c} assay on the ARCHITECT *c* 8000 System.	C.f.a.s. (Calibrator for automated systems) HbA1c is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the enclosed value sheets.
Levels	2 levels (Calibrator 1 and 2) Each lot of calibrators is value-assigned and values are reported in both NGSP and IFCC units. Actual analyte concentrations for each lot of calibrators are listed in the Hemoglobin A_{1c} Calibrator Value Sheet, packaged with the calibrator. The concentration of glycated hemoglobin (HbA_{1c}) and total hemoglobin (THb) is provided for each lot.	1 level The C.f.a.s. HbA1c calibrator is automatically diluted by the system.
Standardization/ Traceability	Calibrators are prepared gravimetrically, lyophilized, and then value assigned using secondary calibrators that are traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) reference method.	This method has been standardized against the approved IFCC reference method for the measurement of HbA1c in human blood and can be transferred to results traceable to DCCT/NGSP by calculation.

Control Similarities and Differences		
Characteristics	**Submission Device Hemoglobin A_{1c}**	**Predicate Device Roche PreciControl HbA1c norm and PreciControl HbA1c path (k103099)**
Intended use	For the estimation of test precision and the detection of systematic analytical deviations of the Hemoglobin A_{1c} assay on the ARCHITECT *c* 8000 System.	For use in quality control by monitoring accuracy and precision for the qualitative methods as specified in the value sheets.
Levels	2 levels (Low and High Control) Lyophilized Assignment of values is specific for each lot.	PreciControl HbA1c norm: 1 level PreciControl HbA1c path:1 level Assignment of values is specific for each lot.
Material	Controls are prepared using hemoglobin and glycated hemoglobin from human whole blood. Prior to lyophilization, the matrix used is MES buffered solution.	PreciControl HbA1c norm is a liquid control based on hemolyzed human blood. The adjusted concentrations of the control components are usually in the normal range or at the normal/pathological threshold. PreciControl HbA1c path is a lyophilized control based on hemolyzed sheep blood. The adjusted concentrations of the control components are usually in the pathological range.

7. Summary of Nonclinical Performance

Within-Laboratory Precision (20-Day)

A 20-day precision study was conducted to evaluate the precision performance of the Hemoglobin A_{1c} assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP5-A2.

Testing was performed using 3 lots of Hemoglobin A_{1c} Reagents, 3 lots of Hemoglobin A_{1c} Calibrators, 1 lot of Hemoglobin A_{1c} Controls (Low and High), and 1 lot of commercially available controls (Control Levels 1, 2, and 3) on 3 ARCHITECT *c* 8000 instruments. The calibration curve generated for each reagent lot was stored on each instrument for the duration of the study. Three levels each of human whole blood controls and human whole blood panels were tested a minimum of 2 replicates, twice per day (separated by a minimum of 2 hours), for a total of 20 testing days. The results for all replicates were reported in both NGSP and IFCC units.

NGSP:

The total imprecision (within-run, between-run, and between-day) by instrument system and reagent lot was as follows for each application:

Whole Blood

- 0.02 to 0.03 SD for Control Level 1
- 0.3 to 0.5 %CV for Control Level 2
- 0.4 to 0.6 %CV for Control Level 3
- 0.02 SD for the panel targeted near 4.0 %HbA_{1c}
- 0.3 to 0.5 %CV for the panel with a target range of 6.0 – 7.0 %HbA_{1c}
- 0.3 to 0.5 %CV for the panel with a target range of 8.0 – 10.0 %HbA_{1c}

Hemolysate

- 0.01 to 0.02 SD for the Hemoglobin A_{1c} Low Control
- 0.3 to 0.5 %CV for the Hemoglobin A_{1c} High Control
- 0.3 to 0.8 %CV for Control Level 3
- 0.02 to 0.03 SD for the panel targeted near 4.0 %HbA_{1c}
- 0.3 to 0.5 %CV for the panel with a target range of 6.0 – 7.0 %HbA_{1c}
- 0.3 to 0.5 %CV for the panel with a target range of 8.0 – 10.0 %HbA_{1c}

Limit of Blank (LoB) and Detection (LoD)

A Limit of Blank (LoB)/Limit of Detection (LoD) study was performed based on guidance from the CLSI document EP17-A.

The zero-level samples were tested in a minimum of 3 replicates and the low-level samples were tested in a minimum of 2 replicates. Five separate runs were performed over a minimum of three days using 2 lots of Hemoglobin A_{1c} Reagents, 2 lots of Hemoglobin A_{1c} Calibrators, and 1 lot of commercially available controls on 2 ARCHITECT *c* 8000 instruments. Each reagent and calibrator lot was tested on each instrument.

The Hemoglobin A_{1c} LoB result is 2.51 %HbA_{1c} (3.89 mmol/mol) and LoD result is 2.52 %HbA_{1c} (4.05 mmol/mol).

Interferences: Endogenous Substances

A study was performed based on guidance from the CLSI document EP7-A2. Interference effects were assessed by comparing test samples containing potentially interfering endogenous substances to reference samples.

The test and reference samples were tested in a minimum of 12 replicates using 1 lot of Hemoglobin A_{1c} Reagents and Calibrators and 1 lot of commercially available controls on 1 ARCHITECT *c* 8000 instrument. The results were reported in both NGSP and IFCC units.

The Hemoglobin A_{1c} assay had a difference within ± 5% for samples ≥ 5.7 %HbA_{1c}. The Hemoglobin A_{1c} assay is not susceptible to interference effects from the following endogenous substances and high test levels:

Endogenous Substance Name	Highest Test Level At Which No Significant Interference Was Observed
Ascorbic Acid	3.0 mg/dL
Conjugated Bilirubin	15.0 mg/dL
Glucose	1000 mg/dL
Triglycerides	3000 mg/dL
Total Protein*	22 g/dL
Unconjugated Bilirubin	10.0 mg/dL
Urea	667 mg/dL
Vitamin E	8.6 mg/dL

* The total protein concentration of 22 g/dL includes serum protein as well as hemoglobin.

Interferences: Hemoglobin Variants

A study was performed based on guidance from the CLSI document EP7-A2.

The samples were tested using 1 lot of Hemoglobin A_{1c} Reagents and Calibrators, 1 lot of Hemoglobin A_{1c} Controls (for the hemolysate application), and 1 lot of commercially available controls (for the whole blood application) on 1 ARCHITECT *c* 8000 instrument. Interference effects were assessed by comparing the Hemoglobin A_{1c} values to reference/expected values for samples containing potentially interfering hemoglobin variants. The results were reported in both NGSP and IFCC units.

No significant interference was observed for the HbC, HbD, HbE, HbS, and HbA2 variants at the levels summarized in the tables below (NGSP units).

Hemoglobin Variant	n	Range in % Abnormal Variant	Range in %HbA_{1c} Concentration
HbC	21	33% - 42%	5.2 - 9.3
HbD	20	35% - 41%	5.2 - 10.7
HbE	20	27% - 32%	5.0 - 10.1
HbS	20	33% - 44%	5.1 - 9.9
HbA2	26	4.7% - 8.5%	4.7 – 13.3
HbF	19	3% - 27.8%	5.2 - 9.0

Hemoglobin Variant	Relative % Bias from Reference/Expected Concentration	
	~ 6.0 %HbA_{1c}	~ 9.0 %HbA_{1c}
HbC	-1.6	-1.9
HbD	-0.8	1.8
HbE	0.0	4.3
HbS	-1.4	4.7
HbA2	-0.6	-0.5
HbF	Bias exceeds -5% when the amount of HbF in the sample exceeds 5% [a]	

[a] A negative bias with HbF is directly proportional in magnitude to the % HbF present in the sample.

NOTE: The presence of multiple variants in a sample may impact the % bias.

For HbF interference, the device has the following prominent boxed warning:

> The Hemoglobin A_{1c} assay has significant interference with the fetal hemoglobin (HbF). Hemoglobin A_{1c} results are invalid for patients with abnormal amounts of HbF, including those with known Hereditary Persistence of Fetal Hemoglobin.

Interferences: Drugs

A study was performed based on guidance from the CLSI document EP7-A2. Interference effects were assessed by comparing test samples containing potentially interfering drugs to reference samples.

The test and reference samples were tested in a minimum of 12 replicates using 1 lot of Hemoglobin A_{1c} Reagents and Calibrators and 1 lot of commercially available controls on 1 ARCHITECT *c* 8000 instrument. The results were reported in both NGSP and IFCC units.

The Hemoglobin A_{1c} assay had a difference within ± 5% for samples ≥ 5.7 %HbA_{1c}. The Hemoglobin A_{1c} assay is not susceptible to interference effects from the following potentially interfering drugs and high test levels:

Drug Name	Highest Drug Level Tested
Acarbose	≤ 50 mg/dL
Acetaminophen	≤ 200 µg/mL
Acetylsalicylate	≤ 50.8 mg/dL
Atorvastatin	≤ 600 µg Eq/L
Captopril	≤ 0.5 mg/dL
Chloropropamide	≤ 74.7 mg/dL
Cyanate	≤ 50 mg/dL
Furosemide	≤ 6.0 mg/dL
Gemfibrozil	≤ 7.5 mg/dL
Ibuprofen	≤ 0.5 mg/mL
Insulin	≤ 450 micro units per mL
Losartan	≤ 5 mg/dL
Metformin	≤ 5.1 mg/dL
Nicotinic Acid	≤ 61 mg/dL
Propranolol	≤ 0.2 mg/dL
Repaglinide	≤ 60 ng/mL

Interferences: Rheumatoid Factor

A study was performed based on guidance from the CLSI document EP7-A2. Interference effects were assessed by comparing test samples containing rheumatoid factor to reference samples.

Each sample was tested in a minimum of 12 replicates using 1 lot of Hemoglobin A_{1c} Reagents and Calibrators and 1 lot of commercially available controls on 1 ARCHITECT *c* 8000 instrument. The results were reported in both NGSP and IFCC units.

The Hemoglobin A_{1c} assay had a difference within ± 5% for samples ≥ 5.7 %HbA_{1c}. The Hemoglobin A_{1c} assay is not susceptible to interference effects from RF less than or equal to 200 IU/mL.

Interferences: Hemoglobin Derivates

A study was performed based on guidance from the CLSI document EP7-A2. Interference effects were assessed by comparing test samples containing the following concentrations of potentially interfering hemoglobin derivatives to reference samples:

- Acetylated Hemoglobin with ≥ 50 mg/dL of ASA (aspirin)
- Carbamlyated Hemoglobin with ≥ 10 mmol/L of Cyanate
- Labile Hemoglobin with ≥ 1000 mg/dL of Glucose

The test and reference samples were tested in a minimum of 12 replicates using 1 lot of Hemoglobin A_{1c} Reagents and Calibrators and 1 lot of commercially available controls on 1 ARCHITECT *c* 8000 instrument. The results were reported in both NGSP and IFCC units.

The Hemoglobin A_{1c} assay had a difference within ± 5% for samples ≥ 5.7 %HbA_{1c}. The Hemoglobin A_{1c} assay is not susceptible to interference effects from acetylated hemoglobin, carbamylated hemoglobin, or labile hemoglobin.

Matrix Comparison

A matrix comparison study was performed to evaluate the blood collection tube types that are suitable for use with the Hemoglobin A_{1c} assay. Specimens with concentration values spanning the measuring interval of the assay were collected from a minimum of 43 different donors in the control tube type (dipotassium EDTA, plastic) and the blood collection tubes under evaluation. The blood collection tubes collected from one individual constituted one sample set.

Each sample was tested in a minimum of 2 replicates using 1 lot of Hemoglobin A_{1c} Reagents and Calibrators and 1 lot of commercially available controls on 1 ARCHITECT *c* 8000 instrument.

The results support the use of the following blood collection tube types with the Hemoglobin A_{1c} assay:

- Dipotassium EDTA, plastic
- Lithium heparin, plastic
- Sodium heparin, plastic
- Sodium Fluoride/Disodium EDTA, plastic
- Tripotassium EDTA, plastic

Linearity

A linearity study was performed based on guidance from the CLSI document EP6-A.

Commercially available linearity sets, comprised of Levels 1, 2, 3, and 4, were obtained. Five additional samples were prepared by combining the 4 levels of the commercially available linearity sets in specific ratios. The 9 samples were tested using the Hemoglobin A_{1c} assay. The 9 samples were tested in a minimum of 2 replicates using 1 lot of Hemoglobin A_{1c} Reagents and Calibrators and 1 lot of commercially available controls on 1 ARCHITECT *c* 8000 instrument. All samples were tested as a set within a single run. The results were reported in both NGSP and IFCC units.

NGSP:

There was no deviation from linearity for samples ranging from 3.5 to 18.1 %HbA_{1c}. The linearity regression analysis results in NGSP units are provided in the table below:

Correlation Coefficient	Intercept	Slope	r2
0.9996	-0.59	0.9782	0.999

IFCC:

There was no deviation from linearity for samples ranging from 14.48 to 173.79 mmol/mol. The linearity regression analysis results in IFCC units are provided in the table below:

Correlation Coefficient	Intercept	Slope	r2
0.9997	-7.23	0.9847	0.999

Method Comparison and Predicted Bias

To demonstrate the assay effectiveness as an aid in the diagnosis of diabetes mellitus, to identify patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus, a method comparison study was performed using an NGSP secondary reference laboratory method (Tosoh HPLC analyzer) as the comparator (reference) method.

The study was performed based on guidance from the CLSI document EP9-A2-IR. A minimum of 120 human whole blood specimens were evaluated with the Hemoglobin A_{1c} assay and the reference method.

For the Hemoglobin A_{1c} assay, the specimens were tested internally in replicates of 2 using 2 lots each of Hemoglobin A_{1c} Reagents and Calibrators, 1 lot of Hemoglobin A_{1c} Controls (for the hemolysate application), and 1 lot of commercially available controls (for the whole blood application) on 2 ARCHITECT *c* 8000 instruments.

The specimens were also tested with an NGSP secondary reference laboratory method in replicates of 2. The specimens were tested over a minimum of 5 days. The results were reported in both NGSP and IFCC units.

NGSP:

Method Comparison

- For the Hemolysate application, the Deming regression slope was 0.99 and the correlation coefficient (r-value) was 0.995 for samples across the measuring interval when comparing the Hemoglobin A_{1c} to the reference method.
- For the Whole Blood application, the Deming regression slope was 1.01 and the correlation coefficient (r-value) was 0.995 for samples across the measuring interval when comparing the Hemoglobin A_{1c} to the reference method.

Predicted Bias

The predicted bias from the regression ranged from -2.5% to -2.7% for the Hemolysate application and -2.4% to -3.0% for the Whole Blood application.

ATD Zone

- For the Hemolysate application, the percentage of observations in the ATD zone was 100.0 (128/128) and the lower limit of the two-sided 95% CI was 97.1%.
- For the Whole Blood application, the percentage of observations in the ATD zone was 99.2 (127/128) and the lower limit of the two-sided 95% CI was 95.7%.

IFCC:

Method Comparison

- For the Hemolysate application, the regression slope was 0.98 and the correlation coefficient (r-value) was 0.996 for samples across the measuring interval when comparing the Hemoglobin A_{1c} to the reference method.
- For the Whole Blood application, the regression slope was 0.99 and the correlation coefficient (r-value) was 0.995 for samples across the measuring interval when comparing the Hemoglobin A_{1c} to the reference method.

Predicted Bias

The predicted bias from the regression ranged from –3.7% to -4.0% for the Hemolysate application and –3.7% to -4.5% for the Whole Blood application.

ATD Zone

- For the Hemolysate application, the percentage of observations in the ATD zone was 96.1% (123/128) and the lower limit of the two-sided 95% CI was 91.2%.
- For the Whole Blood application, the percentage of observations in the ATD zone was 95.3 (122/128) and the lower limit of the two-sided 95% CI was 90.2%.

Total Error Near the Cutoff

Using the results of bias estimation (% Bias) in the method comparison study and precision estimates in the reproducibility study, the Total Error (TE) at four $\%HbA_{1c}$ levels (approximately 5.0%, 6.5%, 8.0%, and 12.0%) was calculated as follows:

$$\%TE = |\%Bias| + 1.96 \times \%CV$$

The results are presented in the tables below.

% Total Error Summary – Hemolysate (NGSP)

%HbA_{1c} Level	Average % Bias	% CV	% TE
5.0	-3.6	0.8	5.2
6.5	-2.8	0.9	4.6
8.0	-2.4	1.0	4.4
12.0	-1.7	1.3	4.2

% Total Error Summary – Whole Blood (NGSP)

%HbA_{1c} Level	Average % Bias	% CV	% TE
5.0	-3.9	0.6	5.1
6.5	-2.9	0.7	4.3
8.0	-2.3	0.7	3.7
12.0	-1.4	1.6	4.5

Measuring Interval

The measuring interval of the Hemoglobin A_{1c} assay is 4.0 to 14.0 %HbA_{1c} (20.22 to 129.51 mmol/mol HbA_{1c}). The limits of the measuring interval were demonstrated through the results of the Within-Laboratory Precision, Tube Type, Linearity, and Method Comparison studies.

Automated Lyse (Whole Blood Application) versus Manual Lyse Methods (Hemolysate Application)

Whole blood specimens are lysed automatically on the ARCHITECT *c* 8000 instrument with the Whole Blood application or may be lysed manually using the Hemoglobin A_{1c} Diluent with the Hemolysate application. The performance of the Hemoglobin A_{1c} automated lyse method versus the manual lyse method was evaluated by testing whole blood specimens using both applications (*i.e.*, Whole Blood and Hemolysate) in the Within-Laboratory Precision and the Method Comparison studies. The results from these studies met the study evaluation criteria and therefore demonstrated acceptable automated and manual lyse methods.

8. Conclusion

The data presented in this premarket notification demonstrates that the Hemoglobin A_{1c} assay performs substantially equivalent to the predicate device, the COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay (k121291). Correlation was demonstrated by comparison to a National Glycohemoglobin Standard Program (NGSP) secondary reference laboratory method.

The data presented in the premarket notification provide reasonable assurance that the Hemoglobin A_{1c} assay is safe and effective for the stated intended use.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

February 28, 2014

ABBOTT LABORATORIES
JUDITH WALLACH
100 ABBOTT PARK RD.
ABBOTT PARK IL 60064-3502

Re: K130255
Trade/Device Name: Hemoglobin A1c
Hemoglobin A1c Calibrators
Hemoglobin A1c Controls
Regulation Number: 21 CFR 862.1373
Regulation Name: Hemoglobin A1c Test System
Regulatory Class: II
Product Code: PDJ, LCP, JIT, JJX
Dated: February 20, 2014
Received: February 21, 2014

Dear Ms. Wallach:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
k130255

Device Name
Hemoglobin A1c / Hemoglobin A1c Calibrators / Hemoglobin A1c Controls

Indications for Use *(Describe)*
The Hemoglobin A1c assay is used in clinical laboratories for the quantitative in vitro measurement of percent hemoglobin A1c (NGSP) or HbA1c fraction mmol/mol (IFCC) in human whole blood and hemolysate on the ARCHITECT c 8000 System. Hemoglobin A1c measurements are used as an aid in the diagnosis of diabetes mellitus, as an aid to identify patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus.

The Hemoglobin A1c Calibrators are for use in the calibration of the Hemoglobin A1c assay on the ARCHITECT c 8000 System.

The Hemoglobin A1c Controls are used for the estimation of test precision and the detection of systematic analytical deviations of the ARCHITECT c 8000 System.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Katherine Serrano -S